DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/18/2011 has been entered.

Claims 1, 3 - 5, 8 - 23, 25, 29, 32 and 36 - 49 are pending.

Claims 8 – 10, 14 – 21, 29, 32, 36 – 37 and 44 – 49 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 04/19/2010.

Maintained formal matters, objections, and/or rejections:

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 4, 12, 13, 25 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Keifer (U. S. Patent No. 5,620,867).

Response to Arguments

Applicants argue that:

> …the rejected claims are drawn to substantially pure BBP, a 2.1 kD peptide derived from the 24 kD phosphoprotein Spp-24. …The claimed BBP and Spp-24 are not the same molecule. …Thus, Keifer does not disclose BBP, much less substantially pure BBP.
>
> …there is no express or inherent evidence that Spp-24 increases the rate or degree of osteogenesis or calcification. …studies have shown that the full length Spp-24 molecule, when combined with BMP, completely inhibits bone formation. …Thus, Keifer cannot anticipate the claimed invention because Keifer does not disclose the BBP, a 2.1 kD peptide that increases the rate or degree of osteogenesis or calcification.
>
> …Keifer does not disclose a substantially purified BBP which increases the degree or rate of osteogenesis or calcification, for example, by BMP-2… because Keifer discloses the much larger Spp-24 protein, which when used in its entirety, inhibits osteogenesis by BMPs. …Keifer does not disclose BBP except as part of the Spp-24 protein. Keifer does not in any way teach that a fragment of the Spp-24 protein disclosed increases the degree or rate of osteogenesis or calcification, including in combination with BMPs. Thus, one skilled in the art reading Keifer would not know that a particular fragment of the protein disclosed will increase the degree or rate of osteogenesis or calcification, for example, by BMPs. In fact, it was unexpected that a fragment derived from Spp-24, which completely inhibits bone formation, would increase the degree or rate of osteogenesis. Thus, Applicants respectfully submit that Keifer does not expressly or inherently disclose all of the elements of the claimed invention, and therefore, Keifer cannot anticipate the claimed invention.
>
> …Applicants have enabled BBP, the claimed fragment of Spp-24 that increases the degree or rate of osteogenesis or calcification by BMP. Despite the fact that the full-length protein Spp-24 contains the sequence for BBP, Spp-24 and BBP are physically in size and conformation different, and as a result do not have the same function. …it is not the case that an amino acid sequence that includes the sequence for BBP will necessarily increase the degree or rate of osteogenesis or calcification.

Applicants' arguments have been fully considered but they are not persuasive. Applicants acknowledge that "Keifer does not disclose BBP except as part of the Spp-24 protein," and "the full-length protein Spp-24 contains the sequence for BBP." Therefore, it appears settled that Keifer discloses a peptide comprising the amino acid sequence of SEQ ID NO: 1. Although the claims encompass the disclosed BPP (SEQ ID NO: 1), the claims, as written, are not limited to the disclosed BPP and do not exclude the Spp-24 protein. Where the claimed and prior art products are identical or substantially identical in structure or composition claimed properties or functions are presumed to be inherent and a prima facie case of anticipation has been established. Therefore, Keifer contains every element of the claimed invention.

The examiner is not making the argument that Spp-24 expressly or inherently increases the degree or rate of osteogenesis or calcification. Nor is it necessary to make such an argument because the claims do not require that the claimed peptide increase the degree or rate of osteogenesis or calcification. Rather, the claims, as written, are not limited to the disclosed BPP (SEQ ID NO: 1) and do not exclude the Spp-24 protein. Therefore, Keifer anticipates the claimed invention.

Insofar as Keifer discloses a peptide comprising the amino acid sequence of SEQ ID NO: 1 (BBP), then Keifer discloses a peptide comprising any and/or all fragments of SEQ ID NO: 1. Although one skilled in art reading Keifer may not know that a particular fragment of the protein disclosed will increase the degree or rate of osteogenesis or calcification, for example, by BMPs, one of skill or ordinary skill would know that Keifer discloses a peptide comprising any and/or all fragments of SEQ ID NO:

1. Therefore, Keifer discloses a peptide comprising a fragment of SEQ ID NO: 1, wherein said fragment increases the degree or rate of osteogenesis or calcification, for example, by BMPs.

Evidence of secondary considerations, such as unexpected results, is irrelevant to 35 U.S.C. 102 rejections and thus cannot overcome a rejection so based.

Although Spp-24 and BBP (SEQ ID NO: 1) may be physically in size and conformation different, and may as a result not have the same function, the claimed peptide is indistinguishable from Spp-24. As mentioned above, the claims do not require that the claimed peptide increase the degree or rate of osteogenesis or calcification.

Claims 1, 3, 4, 12, 13, 22, 25 and 38 – 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Price (WO 96/21006).

Response to Arguments

Applicants argue that Price has similar deficiencies as Keifer. Applicants' arguments have been fully considered but they are not persuasive for the reasons discussed above in reference to Keifer.

Applicants argue that Price teaches the use of the entire Spp-24 peptide, not BBP. Applicants' arguments have been fully considered but they are not persuasive. Although Spp-24 and BBP (SEQ ID NO: 1) may be physically in size and conformation different, and may as a result not have the same function, the claimed peptide is indistinguishable from Spp-24, as discussed above. The claims, as written, are not

limited to the disclosed BPP (SEQ ID NO: 1) and do not exclude the Spp-24 protein, as discussed above. Therefore, Price anticipates the claimed invention.

Response to Amendment

The declaration under 37 CFR 1.132 filed 07/18/2011 is insufficient to overcome the rejection of claims 1 – 4, 12, 13, 25 and 40 under 35 U.S.C. 102(b) based upon Keifer (U. S. Patent No. 5,620,867) and the rejection of claims 1, 3, 4, 12, 13, 22, 25 and 38 – 40 under 35 U.S.C. 102(b) based upon Price (WO 96/21006) as set forth in the last Office action because: The declaration has been considered. However, both Keifer and Price disclose a peptide comprising the amino acid sequence of SEQ ID NO: 1. Although the claims encompass the disclosed BPP (SEQ ID NO: 1), the claims, as written, are not limited to the disclosed BPP and do not exclude the Spp-24 protein, as disclosed by Keifer and Price. Where the claimed and prior art products are identical or substantially identical in structure or composition claimed properties or functions are presumed to be inherent and a prima facie case of anticipation has been established. Therefore, Keifer and Price contain every element of the claimed invention.

Although Spp-24 and BBP (SEQ ID NO: 1) may be physically in size and conformation different, and may as a result not have the same function, the claimed peptide is indistinguishable from Spp-24. As mentioned above, the claims do not require that the claimed peptide increase the degree or rate of osteogenesis or calcification. The claims only require a peptide comprising the amino acid sequence of SEQ ID NO: 1 or a peptide comprising a fragment of SEQ ID NO: 1, wherein said fragment increases the degree or rate of osteogenesis or calcification.

Insofar as Keifer and Price disclose a peptide comprising the amino acid sequence of SEQ ID NO: 1 (BBP), then Keifer and Price disclose a peptide comprising any and/or all fragments of SEQ ID NO: 1. Although one skilled in art reading Keifer or Price may not know that a particular fragment of the protein disclosed will increase the degree or rate of osteogenesis or calcification, for example, by BMPs, one of skill or ordinary skill would know that Keifer and Price disclose a peptide comprising any and/or all fragments of SEQ ID NO: 1. Therefore, Keifer and Price disclose a peptide comprising a fragment of SEQ ID NO: 1, wherein said fragment increases the degree or rate of osteogenesis or calcification, for example, by BMPs.

New formal matters, objections, and/or rejections

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5, 11, 23 and 41 – 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

1. A composition comprising:

(a) a substantially purified peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 1 or a fragment of SEQ ID NO: 1, wherein said

peptide or said fragment increases the degree or rate of osteogenesis by BMP-2 in mammalian cells; and

(b) at least one member selected from the group consisting of a TGFβ family member, BMP-2, BMP-4, BMP-7, or demineralized bone matrix.

2. A medicament for use in inducing the rate or degree of osteogenesis in a vertebrate including:

(a) a substantially purified peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 1 or a fragment of SEQ ID NO: 1, wherein said peptide or said fragment increases the degree or rate of osteogenesis by BMP-2 in mammalian cells; and

(b) a therapeutically effective dosage of one of BMP-2 or demineralized bone matrix.

3. A medicament for use in inducing the rate or the degree of calcification in a vertebrate including a substantially purified peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 1 or a fragment of SEQ ID NO: 1, wherein said peptide or said fragment increases the degree or rate of osteogenesis by BMP-2 in mammalian cells.

4. An article of manufacture comprising a substantially purified peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 1 or a fragment of SEQ ID NO: 1, wherein said peptide or said fragment increases the degree

or rate of osteogenesis by BMP-2 in mammalian cells, immobilized on a solid support, the article of manufacture of further including BMP-2 or demineralized bone matrix.

5. An implant for use in vivo comprising, a substrate having a surface, wherein at least the surface of the implant includes a substantially purified peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 1 or a fragment of SEQ ID NO: 1, wherein said peptide or said fragment increases the degree or rate of osteogenesis by BMP-2 in mammalian cells, wherein the implant further includes one of BMP-2 or demineralized bone matrix, wherein at least the surface of the implant includes at least one of chondrogenic or osteogenic precursor cells, or
wherein the substrate is formed into the shape of a pin, screw, plate, or prosthetic joint;

does not reasonably provide enablement for

6. A composition comprising:
(a) a peptide comprising the amino acid sequence of SEQ ID NO: 1 or a fragment thereof, wherein said fragment increases degree or rate of osteogenesis by BMP-2 in mammalian cells; and
(b) at least one member selected from the group comprising a TGFβ family member, BMP-2, BMP-4, BMP-7, or demineralized bone matrix.

7. A medicament for use in inducing the rate or degree of osteogenesis in a vertebrate including:

(a) a therapeutically effective dosage of a peptide comprising the amino acid sequence of SEQ ID NO: 1 or a fragment thereof, wherein said fragment increases the degree or rate of osteogenesis by BMP-2 in mammalian cells; and

(b) a therapeutically effective dosage of one of BMP-2 or demineralized bone matrix.

8. A medicament for use in inducing the rate or the degree of calcification in a vertebrate including a peptide comprising the amino acid sequence of SEQ ID NO: 1 or a fragment thereof, wherein said fragment increases the degree or rate of calcification in vertebrate cells.

9. An article of manufacture comprising a peptide immobilized on a solid support, wherein said peptide comprises the amino acid sequence of SEQ ID NO: 1 or a fragment thereof, wherein said fragment increases the degree or rate of osteogenesis or calcification by BMP-2, the article of manufacture further including BMP-2 or demineralized bone matrix.

10. An implant for use in vivo comprising, a substrate having a surface, wherein at least the surface of the implant includes a peptide comprising the amino acid sequence of SEQ ID NO: 1 or a fragment thereof, wherein said fragment increases the degree or rate of osteogenesis or calcification by BMP-2, wherein the substrate is formed into the

shape of a pin, screw, plate, or prosthetic joint, wherein said implant further includes one of BMP-2 or demineralized bone matrix, or wherein at least the surface of the implant includes at least one of chondrogenic or osteogenic precursor cells.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are directed to or encompass a peptide comprising the amino acid sequence of SEQ ID NO: 1 or a fragment thereof, wherein said fragment increases the degree or rate of osteogenesis or calcification. The claims, as written, encompass Spp-24, as discussed above. Spp-24 inhibits bone formation. See applicants' response filed 07/18/2011 and the declaration under 37 CFR 1.132 filed 07/18/2011. The specification lacks guidance for using a peptide that inhibits bone formation. For the specification to enable the claimed invention it is incumbent upon applicant to provide the guidance needed to use the claimed composition, implant, medicament or article of manufacture comprising Spp-24. Otherwise the claims are an invitation to experiment.

In view of the breadth of the claims and the limited amount of direction and working examples provided by the inventor, it would require undue experimentation for the skilled artisan to make and/or use the full scope of the claimed invention.

Conclusion

No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 9:00 A.M. TO 5:30 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, JEFFREY STUCKER, CAN BE REACHED AT (571)272-0911.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-0835.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING MAY BE OBTAINED FROM THE PATENT APPLICATION INFORMATION RETRIEVAL (PAIR) SYSTEM. STATUS INFORMATION FOR PUBLISHED APPLICATIONS MAY BE OBTAINED FROM EITHER PRIVATE PAIR OR PUBLIC PAIR. STATUS INFORMATION FOR UNPUBLISHED APPLICATIONS IS AVAILABLE THROUGH PRIVATE PAIR ONLY. FOR MORE INFORMATION ABOUT THE PAIR SYSTEM, SEE HTTP://PAIR-DIRECT.USPTO.GOV. CONTACT THE ELECTRONIC BUSINESS CENTER (EBC) AT 866-217-9197 (TOLL-FREE) FOR QUESTIONS ON ACCESS TO THE PRIVATE PAIR SYSTEM,

/DAVID S ROMEO/
PRIMARY EXAMINER, ART UNIT 1647

DSR
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